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PASSWORD:

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- NEWS 4 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
- NEWS 5 JAN 28 MARPAT searching enhanced
- NEWS 6 JAN 28 USGENE now provides USPTO sequence data within 3 days of publication
- NEWS 7 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment
- NEWS 8 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements
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- NEWS 11 FEB 25 IFIREF reloaded with enhancements
- NEWS 12 FEB 25 IMSPRODUCT reloaded with enhancements
- NEWS 13 FEB 29 WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
- NEWS 14 MAR 31 IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
- NEWS 15 MAR 31 CAS REGISTRY enhanced with additional experimental spectra
- NEWS 16 MAR 31 CA/CAplus and CASREACT patent number format for U.S. applications updated
- NEWS 17 MAR 31 LPCI now available as a replacement to LDPCI
- NEWS 18 MAR 31 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
- NEWS 19 APR 04 STN AnaVist, Version 1, to be discontinued
- NEWS 20 APR 15 WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
- NEWS 21 APR 28 EMBASE Controlled Term thesaurus enhanced
- NEWS 22 APR 28 IMSRESEARCH reloaded with enhancements

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```
=> s (cell-penetrating peptid?)
   2393962 CELL
   2066630 CELLS
   3133503 CELL
        (CELL OR CELLS)
    26237 PENETRATING
    530263 PEPTID?
L1
      618 (CELL-PENETRATING PEPTID?)
        (CELL(W)PENETRATING(W)PEPTID?)
=> s (sc-fv or scfv or (single chain fv))
    50582 SC
     3177 SCS
    53354 SC
        (SC OR SCS)
     7672 FV
     221 FVS
     7765 FV
         (FV OR FVS)
      8 SC-FV
        (SC(W)FV)
     4182 SCFV
     575 SCFVS
     4245 SCFV
        (SCFV OR SCFVS)
    1418057 SINGLE
     3401 SINGLES
   1420946 SINGLE
         (SINGLE OR SINGLES)
    765096 CHAIN
    332456 CHAINS
    960894 CHAIN
        (CHAIN OR CHAINS)
     7672 FV
     221 FVS
     7765 FV
        (FV OR FVS)
     1711 SINGLE CHAIN FV
         (SINGLE(W)CHAIN(W)FV)
L2
      4764 (SC-FV OR SCFV OR (SINGLE CHAIN FV))
=> s L1 and 12
L3
       2 L1 AND L2
```

## L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2005:972196 CAPLUS

DN 143:244215

TI Penetratin Improves Tumor Retention of Single-Chain Antibodies: A Novel Step toward Optimization of Radioimmunotherapy of Solid Tumors

AU Jain, Maneesh; Chauhan, Subhash C.; Singh, Ajay P.; Venkatraman, Ganesh; Colcher, David; Batra, Surinder K.

CS Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE, USA

SO Cancer Research (2005), 65(17), 7840-7846 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

AB Single-chain Fv (scFv) antibody

fragments exhibit improved pharmacokinetics and biodistribution compared with intact IgG. The tumor uptake of scFvs is rapid, and the serum half-life is shorter than IgG. However, scFvs exhibit lower net dose deposition in the tumor due to a shorter residence time that limits their use in radioimmunotherapy. To improve the tumor uptake and retention of scFvs, we investigated the utility of cell-penetrating peptides, penetratin and transactivator of transcription (TAT). Biodistribution studies were done in LS174T tumor-bearing mice with divalent scFv derived from anti-tumor-assocd. glycoprotein 72 monoclonal antibody (mAb) CC49. Penetratin increased the tumor retention of scFvs without affecting the peak dose accumulation. The percentage of doses retained in tumors at 24 h postadministration with a control (no peptide), penetratin, and TAT were 27.25%, 79.84%, and 48.55%, resp., of that accumulated at 8 h postinjection. The tumor-to-blood ratios at 24 h postadministration were 7.14, 19.53, and 16.48 with control, penetratin, and TAT treatment, resp., whereas the pharmacokinetics were unaltered. Coinjection with TAT, however, resulted in increased uptake of the radioconjugate by the lungs. Autoradiog. of the excised tumors indicated a more homogenous distribution of the radiolabeled scFv with both penetratin and TAT in comparison with the control treatment. Real-time whole-body imaging of the live animals confirmed improved tumor localization with penetratin without any increase in the uptake by normal tissues. In conclusion, a significant improvement in the tumor retention of s.c.(Fv)2 was achieved by administration of penetratin. Therefore, the combination of penetratin and scFvs has the potential of improving the utility of mAb-based radiopharmaceuticals.

# RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

#### ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:267364 CAPLUS
DN 140:302337
TI Preparation and use of therapeutic antibodies entering into the cell
IN Valkna, Andres; Kogerman, Priit
PA Inbio Oue, Estonia
SO PCT Int. Appl., 21 pp.
  CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
  PATENT NO.
                    KIND DATE
                                     APPLICATION NO.
                                                            DATE
  PI WO 2004026911
                      A1 20040401 WO 2003-EE5
                                                         20030916
    W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
       CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
       GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
       LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
       OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
       TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
       KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
       FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
       BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
  EE 200200531
                        20040415 EE 2002-531
                                                     20020917
                    Α
  CA 2499321
                   A1
                        20040401 CA 2003-2499321
                                                       20030916
  AU 2003266225
                     A1
                          20040408 AU 2003-266225
                                                         20030916
  EP 1539823
                   A1
                       20050615 EP 2003-797197
                                                      20030916
    R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
       IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
  US 20080063633
                          20080313 US 2005-528073
                     A1
                                                        20050317
PRAI EE 2002-531
                      A
                          20020917
                     W
  WO 2003-EE5
                         20030916
AB The disclosed invention relates to the development of a novel technol. of
  (cancer-)specific antibodies entering into the cell and their use for
  treatment of human diseases (primarily cancer). Such antibody (drug)
  would act by directly modulating the cancer-generating signals. The
  expected effects and principles of action of such antibodies are
  inactivation of intracellular proteins and thus they could be used for the
  treatment of diseases, where the activity of intracellular proteins must
  be modulated for effective treatment (primarily malignant tumors, but also
```

many other diseases, which can be treated by inactivation of intracellular

proteins). The invention relates to the use of peptide vector mols. (cell-penetrating peptides, CPPs), preferably peptide transportan (or its shorter analog transportan TP10), a combination of neuropeptide galanin and wasp venom peptide mastoparan fragments. In examples presented here, these CPPs are conjugated to monoclonal (or polyclonal) antibodies to GLI proteins, assocd. with signaling in basal cell carcinoma pathogenesis. These recombinant antibodies were shown to enter the cultured cells. The same results were obtained when the single-chain (scFv) antibody fragments were used in the recombinant protein.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

## ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s (single chain antibody?)
   1418057 SINGLE
     3401 SINGLES
   1420946 SINGLE
        (SINGLE OR SINGLES)
    765096 CHAIN
    332456 CHAINS
    960894 CHAIN
        (CHAIN OR CHAINS)
    329386 ANTIBODY?
L4
      2130 (SINGLE CHAIN ANTIBODY?)
        (SINGLE(W)CHAIN(W)ANTIBODY?)
=> s L1 and L4
L5
       0 L1 AND L4
=> s (single chain antibod?)
   1418057 SINGLE
     3401 SINGLES
   1420946 SINGLE
        (SINGLE OR SINGLES)
    765096 CHAIN
    332456 CHAINS
    960894 CHAIN
        (CHAIN OR CHAINS)
    522810 ANTIBOD?
L6
      2550 (SINGLE CHAIN ANTIBOD?)
        (SINGLE(W)CHAIN(W)ANTIBOD?)
\Rightarrow s L1 and L6
L7
       1 L1 AND L6
```

# L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

AB Single-chain Fv (scFv) antibody fragments exhibit improved

AN 2005:972196 CAPLUS

DN 143:244215

TI Penetratin Improves Tumor Retention of Single-Chain Antibodies: A Novel Step toward Optimization of Radioimmunotherapy of Solid Tumors

AU Jain, Maneesh; Chauhan, Subhash C.; Singh, Ajay P.; Venkatraman, Ganesh; Colcher, David; Batra, Surinder K.

CS Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE, USA

pharmacokinetics and biodistribution compared with intact IgG. The tumor

SO Cancer Research (2005), 65(17), 7840-7846 CODEN: CNREA8; ISSN: 0008-5472

PB American Association for Cancer Research

DT Journal

LA English

uptake of scFvs is rapid, and the serum half-life is shorter than IgG. However, scFvs exhibit lower net dose deposition in the tumor due to a shorter residence time that limits their use in radioimmunotherapy. To improve the tumor uptake and retention of scFvs, we investigated the utility of cell-penetrating peptides, penetratin and transactivator of transcription (TAT). Biodistribution studies were done in LS174T tumor-bearing mice with divalent scFv derived from anti-tumor-assocd. glycoprotein 72 monoclonal antibody (mAb) CC49. Penetratin increased the tumor retention of scFvs without affecting the peak dose accumulation. The percentage of doses retained in tumors at 24 h postadministration with a control (no peptide), penetratin, and TAT were 27.25%, 79.84%, and 48.55%, resp., of that accumulated at 8 h postinjection. The tumor-to-blood ratios at 24 h postadministration were 7.14, 19.53, and 16.48 with control, penetratin, and TAT treatment, resp., whereas the pharmacokinetics were unaltered. Coinjection with TAT, however, resulted in increased uptake of the radioconjugate by the lungs. Autoradiog. of the excised tumors indicated a more homogenous distribution of the radiolabeled scFv with both penetratin and TAT in comparison with the control treatment. Real-time whole-body imaging of the live animals confirmed improved tumor localization with penetratin without any increase in the uptake by normal tissues. In conclusion, a significant improvement in the tumor retention of s.c.(Fv)2 was achieved by administration of penetratin. Therefore, the combination of penetratin and scFvs has the potential of improving the utility of mAb-based radiopharmaceuticals.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

#### ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s (transport peptide)
    784339 TRANSPORT
     6737 TRANSPORTS
    787076 TRANSPORT
         (TRANSPORT OR TRANSPORTS)
    394289 PEPTIDE
    287255 PEPTIDES
    503184 PEPTIDE
         (PEPTIDE OR PEPTIDES)
L8
       331 (TRANSPORT PEPTIDE)
         (TRANSPORT(W)PEPTIDE)
=> display history
ENTER (BRIEF), FULL, OR NOFILE:brief
ENTER (L1-), L#, OR ?:L1
  (FILE 'HOME' ENTERED AT 11:33:08 ON 17 MAY 2008)
  FILE 'CAPLUS' ENTERED AT 11:33:26 ON 17 MAY 2008
L1
       618 S (CELL-PENETRATING PEPTID?)
=> se L8 and (sc-fv or scfv or (single chain antibod?))
SE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
=>
=> s L8 and (scfv or sc-fv or (single chain antibod?))
     4182 SCFV
     575 SCFVS
     4245 SCFV
         (SCFV OR SCFVS)
    50582 SC
     3177 SCS
    53354 SC
         (SC OR SCS)
     7672 FV
     221 FVS
     7765 FV
         (FV OR FVS)
       8 SC-FV
```

```
(SC(W)FV)
   1418057 SINGLE
     3401 SINGLES
   1420946 SINGLE
        (SINGLE OR SINGLES)
    765096 CHAIN
    332456 CHAINS
    960894 CHAIN
        (CHAIN OR CHAINS)
    522810 ANTIBOD?
     2550 SINGLE CHAIN ANTIBOD?
        (SINGLE(W)CHAIN(W)ANTIBOD?)
L9
       0 L8 AND (SCFV OR SC-FV OR (SINGLE CHAIN ANTIBOD?))
=> s (membrane transport peptide)
    792691 MEMBRANE
    340529 MEMBRANES
    885590 MEMBRANE
        (MEMBRANE OR MEMBRANES)
    784339 TRANSPORT
    6737 TRANSPORTS
    787076 TRANSPORT
        (TRANSPORT OR TRANSPORTS)
    394289 PEPTIDE
    287255 PEPTIDES
    503184 PEPTIDE
        (PEPTIDE OR PEPTIDES)
L10
       17 (MEMBRANE TRANSPORT PEPTIDE)
        (MEMBRANE(W)TRANSPORT(W)PEPTIDE)
=> s L10 and (scfv or scfv or single chain antibod?)
     4182 SCFV
     575 SCFVS
    4245 SCFV
        (SCFV OR SCFVS)
     4182 SCFV
     575 SCFVS
    4245 SCFV
        (SCFV OR SCFVS)
   1418057 SINGLE
     3401 SINGLES
   1420946 SINGLE
        (SINGLE OR SINGLES)
    765096 CHAIN
    332456 CHAINS
    960894 CHAIN
```

(CHAIN OR CHAINS)
522810 ANTIBOD?
2550 SINGLE CHAIN ANTIBOD?
(SINGLE(W)CHAIN(W)ANTIBOD?)
L11 0 L10 AND (SCFV OR SCFV OR SINGLE CHAIN ANTIBOD?)